REMARKS

In the Office Action of July 12, 2007, the Examiner objected to claims 46-48 for the informality that the active step of injecting the vaccine was not included. Applicants have adopted the language the Examiner kindly suggested.

Claims 46-48 stand rejected under 35 U.S.C.§ 112, second paragraph, for being indefinite. The Examiner objected to the phrase "significant injection site lesion formation." The Examiner asserted that the meets and bounds of what is significant are not defined. Applicants traverse the Examiner's objection as the skilled practitioner familiar with injection site lesions and product loss resulting therefrom would clearly understand the meaning of that term. However, in order to advance the prosecution of this application the claims have now been amended to recite that the injection site lesion formation is reduced at least 40% compared with an injection of 5 ml of said vaccine. The claims are also, in this regard, amended to recite that the amount injected is about 2 ml. Support for these amendments is found in the specification in Example 8, beginning on page 52. In Tables 12 and 13 associated therewith, an approximately 41% reduction in lesions is reported (see Table 12, page 54, reduction incident of lesions after weaning from 79.5% to 46.3%). The term "at least 40%" is further supported in Table 14 on page 55, which reports a reduction of more than 56% when using a 2 ml dose as compared with a 5 ml dose.

The Examiner has also suggested that in the claims we use the phrase "a protective antigen component" rather "the protective antigen component…". This amendment has also been made.

Claims 46-48 stand rejected under 35 U.S.C. § 103(e) for being obvious over Roberts taken in view of Lund. Roberts is said to teach a multicomponent clostridial vaccine and an adjuvant, as well as teaching that non-clostridial antigens such as *Moraxella bovis* are added to the multicomponent vaccines, and that the bacterins and toxoids are administered in vaccine compositions including readily dispersible soluble adjuvants thereby avoiding chronic irritation

at the injection site. The Examiner has stated that Roberts teaches that dispersible, soluble adjuvants exhibit low tissue reactivity, and that the vaccines are administered without harmful side effects and chronic inflammatory responses that produce granulomas and abscesses. The Examiner stated that Roberts discloses that other potent adjuvants have been used with clostridial vaccines including CARBOPOL™ polymers. The Examiner acknowledged, however, that Roberts does not specifically recite an encapsulating polymer adjuvant, whereby the encapsulating polymer adjuvant releases antigens slowly at the site of injection without significant permanent injection site lesion formation.

Lund is relied on for teaching that an adjuvant polymer, such as CARBOPOL™, is retained at the site for prolonged slow release and acts by absorbing the active agent into the polymer.

The Examiner concluded that it would have been prima facie obvious to apply the encapsulating polymer of Lund to Roberts' method of immunizing cattle in order to avoid irritation and significant lesion formation at the injection site. It is alleged that no more than routine skilled would have been required to exchange the readily dispersible adjuvants of Roberts for the commercially available and functionally equivalent encapsulating polymer adjuvant of Lund since Lund teaches that adjuvant polymers are retained at the injection site for prolonged slow release of antigens, and that it would have been prima facie obvious to combine the invention of Roberts and Lund to advantageously achieve low tissue reactivity within the cattle and avoid chronic inflammatory responses, granulomas and abscesses.

The rejection over Roberts and Lund is respectfully traversed. It could not have been obvious to substitute the encapsulating polymer of Lund in the composition of Roberts. Roberts teaches against using encapsulating polymers. In the Examiner's words "Roberts teaches the bacterins and toxoids are administered in vaccine compositions including readily dispersible soluble adjuvants thereby avoiding chronic irritation at the injection site (page 6, lines 13-15). Roberts teaches that the dispersible, soluble adjuvants exhibit low tissue reactivity (page 4, line

26-28)."

That is, Roberts teaches that low tissue reactivity is accomplished using dispersible, soluble adjuvants. Roberts teaches against using encapsulating adjuvants, such as those used in the present invention.

On page 1, the first full paragraph, Roberts states:

> "The present invention relates generally to vaccine compositions and methods of using the same. More specifically, the invention pertains to multicomponent clostridial vaccines **made without** (emphasis added) stabilizing carriers or **depot adjuvants** (emphasis added), but rather with a readily dispersible, water-soluble adjuvant, saponin."

On page 2, the paragraph beginning on line one, Roberts recites:

> "Other potent **depot adjuvants** (emphasis added), such as water-in-oil emulsions and carbopol, have also been used in clostridial vaccines. The above-described adjuvants, although increasing antigenicity, **usually provoke severe persistent local reactions** (emphasis added), such as granulomas, abscesses and scarring, when injected subcutaneously or intramuscularly. These local reactions are, in turn, responsible for carcass blemish which requires expensive trimming, a consideration when the vaccine has been injected into muscle tissue destined to be a valuable cut of meat."

On page 2, in the paragraph beginning on line 22, Roberts recites:

> "The present invention is based on the surprising discovery that the water-soluable adjuvant, saponin, can be used in place of a depot adjuvant in multicomponent clostridial vaccines for cattle."

On page 4, in the paragraph beginning on line 24, Roberts states:

> "**Central to the present invention is the surprising discovery** (emphasis added) that stable, potent, multicomponent clostridial vaccines can be made **without the use of depot adjuvants** (emphasis added). In particular, the present invention provides for vaccines including rapidly dispersed, soluble adjuvants, that is, **adjuvants that are not retained at the injection site for a significant period of time, thereby exhibiting low tissue reactivity** (emphasis added). The vaccines can be administered intramuscularly and subcutaneously without the harmful side effects and chronic inflammatory responses that produce granulomas and abscesses, seen with other clostridial vaccine compositions when administered via these routes."

Roberts clearly teaches against using an encapsulating polymer adjuvant that releases antigens slowly at the site of injection. Any skilled practitioner reading Roberts would conclude that using such polymer adjuvants would result in high incidents of "severe persistent local reactions, such as granulomas, abscesses and scarring," that would in turn be "responsible for carcass blemish which requires expensive trimming." Applicants teach using such encapsulating polymer adjuvants and achieve the minimization of injection cite lesion formation (a reduction of at least 40%) by administering 2 ml doses rather than conventional 5 ml doses.

The ordinary practitioner would never, based on the teaching of Roberts, exchange the adjuvant of Roberts for an equivalent encapsulating polymer, as Roberts clearly teaches that such polymer adjuvants result in deleterious injection site lesion formation. Roberts does not suggest in any way that these problems could be overcome with low dose encapsulating polymer formulations.

In view of the clear teaching by Roberts to not use encapsulating polymers, the ordinary practitioner would never combine the teachings of Roberts and substitute an encapsulating polymer in view of Lund. Following the teaching of Lund, using a prolonged release polymer adjuvant, would be expected, based on Roberts, to "provoke severe persistent local reactions,

such as granulomas, abscesses and scarring,..." that "are, in turn, responsible for carcass blemish...." (page two, first paragraph). The ordinary practitioner, reading Roberts, would never adopt the use of the adjuvant polymers, at any dosage, taught by Lund.

In view of the above it is believed that claims 46, 47, and 48, as now amended, are in condition for allowance. Favorable action is solicited. Should the Examiner consider that a conference would be helpful in advancing the prosecution of this application, she is invited to telephone the Applicants' attorney at the number below.

Applicants do not believe that any other fee is due in connection with this filing. If, however, Applicants do owe any such fee(s), the Commissioner is hereby authorized to charge the fee(s) to Deposit Account No. 02-2334. In addition, if there is ever any other fee deficiency or overpayment under 37 C.F.R. §1.16 or 1.17 in connection with this patent application, the Commissioner is hereby authorized to charge such deficiency or overpayment to Deposit Account No. **02-2334**.

Respectfully submitted,

William M. Blackstone, PTO Reg. No. 29772
Chief Patent Counsel
Patent Department
Intervet Inc.
P.O. Box 318
29160 Intervet Lane
Millsboro, DE 19966
(302) 934-417 (tel)
(302) 934-4305 (fax)